



US007378508B2

(12) **United States Patent**
Chiu et al.

(10) **Patent No.:** **US 7,378,508 B2**
(45) **Date of Patent:** **May 27, 2008**

(54) **POLYMORPHIC CRYSTALLINE FORMS OF TIACUMICIN B**

(75) Inventors: **Yu-Hung Chiu**, San Diego, CA (US);
Tessie Mary Che, San Diego, CA (US);
Alex Romero, San Diego, CA (US);
Yoshi Ichikawa, San Diego, CA (US);
Youe-Kong Shue, Carlsbad, CA (US)

(73) Assignee: **Optimer Pharmaceuticals, Inc.**, San Diego, CA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **11/831,886**

(22) Filed: **Jul. 31, 2007**

(65) **Prior Publication Data**

US 2007/0259949 A1 Nov. 8, 2007

Related U.S. Application Data

(63) Continuation-in-part of application No. PCT/US2005/002887, filed on Jan. 31, 2005.

(60) Provisional application No. 60/881,950, filed on Jan. 22, 2007.

(51) **Int. Cl.**

C07H 17/08 (2006.01)

C07D 313/00 (2006.01)

(52) **U.S. Cl.** **536/7.1**; 549/271

(58) **Field of Classification Search** None
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

3,978,211 A * 8/1976 Coronelli et al. 424/120
4,918,174 A 4/1990 McAlpine et al.
5,583,115 A 12/1996 McAlpine et al.
5,767,096 A 6/1998 Hochlowski et al.
2006/0257981 A1 * 11/2006 Shue et al. 435/124
2007/0173462 A1 * 7/2007 Shue et al. 514/28

FOREIGN PATENT DOCUMENTS

WO WO 2004/014295 2/2004
WO WO2004/014295 * 2/2004

WO WO 2005/112990 12/2005

OTHER PUBLICATIONS

Chemical Abstracts registry entry 56645-60-4, Tiacumicin B, Copyright 2007, American Chemical Society, p. 1-2.*

Braga et al., "Making crystals from crystals: a green route to crystal engineering and polymorphism" Chemical Communications (2005) pp. 3635-3645.*

Pharmaceutical Dosage Forms: Tablets, vol. 2, Published by Marcel Dekker, Inc., ed. by Lieberman, Lachman, and Schwartz, pp. 462-472.*

Dean, J., Analytical Chemistry Handbook, Published by McGraw-Hill, Inc., pp. 10.23-10.26.*

Jain et al., "Polymorphism in Pharmacy" Indian Drugs (1986) vol. 23, No. 6, pp. 315-329.*

The Condensed Chemical Dictionary, Tenth Edition, published 1981 by the Van Nostrand Reinhold Company, revised by Gessner G. Hawley, p. 35 and 835.*

Polymorphism in Pharmaceutical Solids, published 1999 by Marcel Dekker Inc, ed. by Harry G. Brittain, pp. 1-2.*

Robert N. Swanson et al., In Vitro and In Vivo Evaluation of Tiacumicins B and C against *Clostridium difficile*, *Antimicrob. Agents Chemother.*, Jun. 1991, pp. 1108-1111.

J.E. Hochlowski et al., Tiacumicins, A Novel Complex of 18-Membered Macrolides, *J. Antibiotics*, vol. XL, No. 5, pp. 575-588 (May 1987).

* cited by examiner

Primary Examiner—Shaojia Anna Jiang

Assistant Examiner—Eric S Olson

(74) *Attorney, Agent, or Firm*—Morgan Lewis & Bockius LLP

(57) **ABSTRACT**

The invention relates to novel forms of compounds displaying broad spectrum antibiotic activity, especially crystalline polymorphic forms and amorphous forms of such compounds, compositions comprising such crystalline polymorphic forms and amorphous forms of such compounds, processes for manufacture and use thereof. The compounds and compositions of the invention are useful in the pharmaceutical industry, for example, in the treatment or prevention of diseases or disorders associated with the use of antibiotics, chemotherapies, or antiviral therapies, including, but not limited to, colitis, for example, pseudo-membranous colitis; antibiotic associated diarrhea; and infections due to *Clostridium difficile* ("C. difficile"), *Clostridium perfringens* ("C. perfringens"), *Staphylococcus* species, for example, methicillin-resistant *Staphylococcus*, or *Enterococcus* including Vancomycin-resistant *enterococci*.

20 Claims, 3 Drawing Sheets